data, the confounding effects of hemolysis on the interpretation of serial changes in troponins vary according to what assay is being used. Laboratories should be aware of the influence of hemolysis and should offer caveats regarding potential interference when appropriate.

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High-Sensitivity Cardiac Troponin: Seeing the Wood from the Trees

To the Editor:

The perspective provided by Jaffe and Apple (1) regarding the landmark publications in The New England Journal of Medicine offers an insightful commentary regarding the clinical utility of the so-called high-sensitivity cardiac troponin assays (2, 3).

We fully support the notion that many of the assays evaluated in these papers should be considered contemporary rather than high-sensitivity. The scorecard categorization is a valuable tool for any clinical laboratory to assess the analytical performance of their troponin assay (4). Jaffe and Apple incorrectly referenced the high-sensitivity cardiac troponin T (hs-cTnT) (Roche) in the study of Keller et al. (2, 3).

In reviewing the Keller et al. article (2) and the supplementary methods (available as an online appendix), we observed that the authors used the current fourth-generation cTnT assay rather than the hs-cTnT assay for comparison between methodologies.

It is interesting to note that the diagnostic utility of the Abbott cTnI, the Roche standard cTnT, and developmental cTnI assays is superior when using the 99th percentile cutoff rather than the 10% coefficient of variation, at the cost of specificity (3). Diagnostically, they perform as well as the hs-cTnT, calling into question the true sensitivity of this assay. Many clinical laboratory specialists favor the 10% coefficient of variation cutoff value over the 99th percentile, presumably as this is within a margin of safety with which they are both familiar and comfortable and that is applied to other immunoassay tests.

The drive to use the 99th percentile is warranted, as demonstrated by the studies of Keller et al. and Reichlin et al. (2, 3); however, the real challenge to adequately assess clinical sensitivity and specificity will come from prospective studies of unselected chest pain patients presenting to the emergency department.

The newer hs-cTn assays in development may prove to be superior diagnostically. Analytically, both the contemporary and high-sensitive assays challenge the performance of current immunoassay technology. The development of other detection methods such as single-molecule-counting technology may be the appropriate alternative (5), if this technology can be adapted for large high-throughput analyzers with reduced turnaround time without compromising analytical performance.

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Comment on “High-Sensitivity Cardiac Troponin: Hype, Help, and Reality”

To the Editor:

We thank Jaffe and Apple (1) for their interest in our study. In their perspectives on details of our study and the study by Keller et al., which were both published recently in the New England Journal of Medicine (2, 3). Although we fully agree with several of their statements, we strongly disagree with others. It is
detrimental to the much-needed interdisciplinary discussion on the best possible clinical use of sensitive cardiac troponin assays when the discussion is based on incorrect statements. Unfortunately, the Jaffe and Apple perspective contains 2 important errors.

First, and of most importance, Jaffe and Apple (1) asked, “How did these studies deal with the problem of increased [cardiac troponin] concentrations produced by diseases other than acute myocardial infarction (AMI)?” and stated, “Not very well. For the most part, the authors . . . used a [cardiac troponin] concentration above the cutoff value as the sole criterion for the diagnosis of acute coronary syndrome (ACS).” They also stated, “The presence of a changing . . . pattern, which is an essential part of the criteria for the diagnosis of AMI in all the guide-
lines, was used in only a subset of patients in the Reichlin et al. article . . . .” These statements are incorrect in 2 respects. On the other hand, AMI was defined in our study in all patients in full agreement with the current universal definition of AMI (4), which requires evidence of myocardial necrosis with a changing pattern associated with clinical signs of myocardial ischemia, as stated clearly in the Method section of our report (2). Necrosis was diagnosed on the basis of a rising and/or falling pattern of the cardiac troponin concentration, with at least 1 value above the 99th percentile at a level of imprecision of <10% (2). On the other hand, noncoronary conditions that increased cardiac troponin concentrations according to conventional cardiac troponin assays were not called “true positives” but were included in the diagnostic group “cardiac symptoms from causes other than coronary artery disease” (2). Ninety-five (13%) of 718 patients were adjudicated in this group, and 16 of these patients had acute cardiac necrosis of an origin other than coronary artery disease (e.g., myocarditis, tachyrhythmias, or acute heart failure).

Second, Jaffe and Apple (1) argue that the incidence of ACS is much lower in the US than the incidence reported in the 2 studies published in the New England Journal of Medicine (2, 3) and state that the incidence of ACS was 46% in our study. This statement is incorrect. The incidence of ACS in our study as reported in the Results section of the report was 33% (2). In addition, results from a recently completed multicenter study that included consecutive patients presenting to the emergency department with symptoms suggestive of AMI showed that the difference in the incidence of local emergency department diagnosis of ACS among centers in the US [range, 4%–40%; data on file at FAST-TRAC Data Management Center, San Diego, CA (Dr. Greg Shipp, Nanosphere, personal communication, January 15, 2010)] was greater by far than potential differences between the US and Europe. Therefore, we think that the disease incidence encountered in an individual emergency department is predominantly determined by the details of the local patient flow, such as a competing high-volume catheterization laboratory in a neighboring hospital that receives most high-risk and high-probability ambulance cases, or such as local hospital standards that guide chest pain patients only to the emergency department as long as they are perceived as low risk and low probability and that triage all high-probability patients directly to a coronary care unit.

We hope that these clarifications help to advance the important